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AGILENT TECHNOLOGIES, INC. INTELLECTUAL PROPERTY ADMINISTRATION, LEGAL DEPT. P.O. BOX 7599 M/S DL429 LOVELAND, CO 80537-0599			ART UNIT 1637	PAPER NUMBER

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**GROUP 1600**

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 09/836,012  
Filing Date: April 17, 2001  
Appellant(s): SAMPSON ET AL.

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Cynthia J. Lee  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed January 23, 2006 appealing from the Office action mailed on August 23, 2005.

**(1) Real Party in Interest**

A statement identifying by name the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The statement of the status of claims contained in the brief is correct.

**(4) Status of Amendments After Final**

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

WO 95/04160	SOUTHERN et al.	02-1995
US 6,607,878	SORGE, JOSEPH A	08-2003
US 5,654,413	BRENNER, SYDNEY	08-1997

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

A. Claims 1-17, 74-83 rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al. (WO 95/04160) in view of Sorge (USPN. 6,607,878).

Southern et al. teach a composition (mixture) of claims 1-2, 7, 12, 14, 81-82, comprising X-mer precursor having a minimum length of 6 nucleotides (see page 5, line 28-36, page 55, line 13-23, page 2, line 27-33), wherein the mixture the mixture has at least complexity of at least  $56/N$ , wherein N represents the number of distinct X-mers (see page 5, line 28-36, Fig. 3a, page 55, line 13-23); wherein the mixture comprises a set of tags (reporter groups) and each tag is covalently linked to at least one X-mer through a cleavable linkage (see page 6, paragraph 2, page 7, line 3-6, page 14, line 1-24).

With regard to claims 2, Southern et al. also teach that X-mer precursors comprise isotopic composition (see page 7, line 3-12);

With regard to claims to claims 3-6, Southern et al. teach 4096 different hexanucleotides with known oligonucleotide sequences (which includes sets of X-mers ranging from 128 to 512) (see page 5, line 28-30, page 42, line 1-30);

With regard to claim 7, Southern et al. teach that the number tags distinguishable by mass spectrometry includes 20- 4096 (each X-mer having a unique tag) (see page 5, line 28-30, page 2, lines 27-33);

With regard to claims 8-11, Southern et al. teach that 4096 number of unique tags (which includes the number ranging from 10-5000) (see page 5, line 28-30);

With regard to claim 12-17, 83, Southern et al. teach that said number of tags is greater than a mass complexity of a natural equivalent (without a tag) and the increment in adding a reporter is larger than the mass difference between the smallest and the largest tag (page 7, line 27-35, page 8, table 2, that indicates 0.5%-100% number of tags).

However Southern et al. did not specifically teach any oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight, tags distinguishable by mass spectrometry and kit comprising said mixture of X-mer precursors.

Sorge et al. teach collection of uniquely tagged molecules wherein Sorge teach the use of oligonucleotide tags, each with discrete molecular weight (see col. 22, line 56-67, col. 23, line 1-6). Sorge also teaches that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also teaches tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the mixture of X-mer precursors as taught by Southern et al. with a step of using tags with discrete molecular weight as taught by Sorge for the purpose of enriching tagged precursors by targeting size differences in oligonucleotide tags to provide an efficient sorting of DNA fragments in a mixture. One skilled in the art would be motivated to combine the mixture of x-mers as taught by Southern et al. with the inclusion molecular weight tags as taught by as taught by Sorge because Sorge explicitly taught that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and

provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also explicitly taught tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67). An ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags would result in enriching sequence information of any oligonucleotide of interest in the mixture, further incorporating tags that are distinguishable by mass spectrometry would enhance the sensitivity of the detectable mass tags and improve the identification of sequence information. And packaging the collection tagged molecules in a kit format would result in a cost-effective and ready to use x-mer precursors for various molecular analysis and such modification of the X-mer mixture would be obvious over the cited prior art in the absence of secondary considerations.

B. Claims 1, 3-6, 74-80 are rejected 35 U.S.C. 103(a) as being unpatentable over Brenner (USPN. 5,654,413) in view of Sorge (6,607,878).

Brenner teaches a composition (mixture) of claims 1, 3-5, comprising X-mer precursor having a minimum length of 3 nucleotides (see col. 3, line 15-67, col. 4, line 1-8, col. 7, line 39-60), wherein the mixture the mixture has at least complexity of at least  $56/N$ , wherein  $N$  represents the number of distinct X-mers (see col. 7, table II shows complexity of at least  $56/N$ ); wherein the mixture comprises a set of tags and each tag is covalently linked to at least one X-mer through a cleavable linkage (see col. 9, line 25-67, col. 10, line 1-67, col. 11, line 1-65).

With regard to claim 6, Brenner teaches that the nucleotide sequences of the precursors of said mixture are known (see col. 7, table II);

With regard to claims 74-80, Brenner teaches a kit composition comprising said mixture of x-mer precursors (comprising natural or non-natural nucleotides, see col. 5, line 37-44), enzymes such as polymerases (polymerases are also considered as condensing agent herein, since the instant specification did not define the term condensing agent nor given any specific examples of a condensing agent), ligases, an array comprising surface and multiplicity of sequence probes (oligonucleotides) attached to it (see col. 23, line 40-57, col. 17, line 35-63, col. 18, line 43-67).

However Brenner did not specifically teach any oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight, tags distinguishable by mass spectrometry

Sorge et al. teach collection of uniquely tagged molecules wherein Sorge teach the use of oligonucleotide tags, each with discrete molecular weight (see col. 22, line 56-67, col. 23, line 1-6). Sorge also teaches that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also teaches tags that are distinguishable by mass spectrometry and a kit comprising said mixture of DNA fragments (see col. 27, line 10-67).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the mixture of x-mer precursors as taught by Brenner with a step of using tags with discrete molecular weight that are distinguishable by mass spectrometry as taught by Sorge for the purpose of enriching tagged precursors by targeting size differences in oligonucleotide tags to provide an efficient and sensitive sorting of DNA fragments in a mixture.

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One skilled in the art would be motivated to combine the mixture of X-mers as taught by Brenner with the inclusion molecular weight tags as taught by Sorge because Sorge explicitly taught that the use of molecular weight tags would allow for unambiguous identification of molecular weight after cleavage and provide sequence information of each DNA fragment in a given restriction pattern and identification of any particular nucleotide sequence in the mixture (see col. 23, line 1-22). Sorge also explicitly taught tags that are distinguishable by mass spectrometry (see col. 27, line 10-67). An ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags that are distinguishable by mass spectrometry would result in enriching sequence information of any oligonucleotide of interest in the mixture and sensitivity of the detectable tags in identifying the sequence information, and such modification of the X-mer mixture would be obvious over the cited prior art in the absence of secondary considerations.

**(10) Response to Argument**

issue

Does the broad recitation of mixture or set of sub-mixtures comprising X-mer precursors distinguishable over the cited prior art?

Introduction

The instant claims are drawn to a mixture or set of sub-mixtures comprising X-mer precursors, wherein X-mer precursors have a minimum length of 3 nucleotides and minimum coverage complexity of at least  $56/N$ , wherein the mixture or sub-mixtures further comprise a set of tags that are distinguishable by mass spectrometry and any given oligonucleotide sequence in the mixture is attached to preferably a single tag with a discrete molecular weight. Thus the



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invention is basically drawn to a mixture comprising mass tagged X-mer precursors with minimum coverage complexity 56/N or to a sub-mixture comprising a plurality of mass tagged X-mer precursors with minimum coverage complexity of 56/N.

#### Broadest Reasonable Interpretation

Appellant relies heavily on the recitation of sub-mixtures and asserts that the prior art of the record does not teach or suggest said limitations. As noted in MPEP 2111 [R-1] the instant claims are given the Broadest Reasonable interpretation consistent with the specification.” In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Thus the broad recitation of a mixture is given the broadest reasonable interpretation because the claims are in open “comprising” format, the mixture can be interpreted as having any additional sub-mixtures. The claims require either a mixture comprising X-mer precursors or a set of sub-mixtures comprising X-mers, which can be interpreted as a mixture having sub-mixtures or a mixture comprising a set of sub-mixtures. Thus the broad recitation of a set of sub-mixtures basically are part of a mixture.

#### *Basis for Prima Facie Case*

The obviousness rejection is based on two independent rejections as Southern et al. in view of Sorge et al. and Brenner et al. in view of Sorge et al. Both the rejections address the obviousness to combine the teachings of a mixture comprising X-mer precursors with a mass tag to obtain a discrete size ladder that can be detectable by a mass spectrometer. Use of mass tags or labels for the purpose of enhancing the sensitivity of detecting single base variations based on molecular mass is well known in the molecular biology art as exemplified by Sorge et al. reference. Thus it is obvious to modify a mixture comprising X-mer precursors as taught by

Southern et al. or Brenner et al. with a mass tag attached to X-mer precursors as discussed in the rejections above.

On page 5-7 of the appeal brief, Appellants argue that Southern et al. teach a mixture of 4096 hexanucleotides, however Southern et al. does not teach or suggest a mixture or set of sub-mixtures as required by the independent claims and refer to the specification for specific features of said mixture. Appellants' arguments are fully considered however as noted in the MPEP. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The limitations upon which the arguments are based, are not present in the claims. Further the broader recitation of a mixture or sub-mixtures of x-mer precursors does not distinguish the instant claims over the mixture taught by Southern et al.

On page 7-9 of the appeal brief, Appellants argue that as admitted by the office Southern et al. does not teach a single tag with a discrete molecular weight distinguishable by mass spectrometry and Sorge et al. does not remedy this deficiency. Appellants also argue that the tags that are multiples of four or blocks of colors taught by Sorge et al. are not equivalent to the instantly claimed tags with discrete molecular weight and assert that the tags with different molecular mass as taught by Sorge et al. are not tags with discrete molecular weight. Appellants' arguments are fully considered, however the instant claims reciting any given oligonucleotide is attached to preferably single tag with discrete molecular weight, does not distinguish from the mass tags with multiples of four as taught by Sorge et al. because the mass tags taught by Sorge et al. does represent 4096 different primer combinations in each pool, wherein each oligonucleotide also differs in sequence thus the overall molecular mass of each primer depends

on the sequence of the oligonucleotide + the mass tag used, giving rise to a discrete molecular mass of any given oligonucleotide in the pool.

Appellants further assert that the independent claims are not obvious over the combination of Southern et al. and Sorge and the dependent claims also non-obvious for lack of teachings of a kit and enzymes in either reference. In response to the assertions Examiner notes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, specific motivation is provided in the rejection, which states that an ordinary artisan would have a reasonable expectation of success that inclusion of discrete molecular weight tags would result in enriching sequence information of any oligonucleotide of interest in the mixture, further incorporating tags that are distinguishable by mass spectrometry would enhance the sensitivity of the detectable mass tags and improve the identification of sequence information. And packaging the collection tagged molecules in a kit format would result in a cost-effective and ready to use X-mer precursors for various molecular analysis and such modification of the X-mer mixture would be obvious over the cited prior art in the absence of secondary considerations.

On page 9-12 of the appeal brief, Appellants assert that the combination of Brenner and Sorge et al. does not teach or suggest the instant invention. Appellants assert that the office has interpreted oligonucleotide tags as X-mer precursors and provides their own lexicographer to define the term "tag" and argue that the oligonucleotide tags do not represent X-mer precursors.

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Appellants further argue that applicant chose his own lexicographer and defined the terms in the specification, thus the claims are to be compared to the prior art based on the defined claim terms. Examiner notes that the claims do not exclude oligonucleotide tag as X-mer precursors because the tag definition clearly excludes the oligonucleotide sequence tags as a tag in their own lexicographer terminology, and the oligonucleotide sequence tags taught by Brenner are within the scope of X-mer precursors and note that the prior art terms are within the scope of the defined terms and thus the oligonucleotide tags are within the scope of the X-mer precursors.

#### Conclusion

Therefore, for the above reasons, the rejections under U.S.C. 103(a) should be sustained.

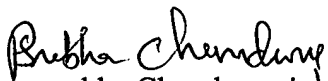
#### (11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

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